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TOBACCO INDUSTRY RESEARCH COMMITTEE
150 EAST FORTY SECOND STREET NEW YORK 17, N. Y.

Application For Research Grant

Date: October 9, 1958

1. Name of Investigator: J. Alfred Rider, M. D., Ph.D.

2. Title: Assistant Professor of Medicine; Assistant Chief, Gastrointestinal Clinic, Department of Medicine.

3. Institution & Address: University of California Medical Center
San Francisco 22, California

4. Project or Subject: The Effects of Tobacco Smoke on Gastric Secretion

We propose to do a thorough study to determine whether or not the tobacco smoke from cigarettes increases gastric acidity, gastric pepsin, or gastric uropepsin. We would also like to clinically evaluate ulcer patients to determine whether their ulcers were aggravated by smoking.

Included in this study would be a comparison of the effects on gastric secretion of two major brands of filter and non-filter cigarettes.

5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

A group of 10-20 patients without organic disease and a group of 10-20 patients with gastric or duodenal ulcer would be used for each brand of cigarettes with and without filters. After a basal gastric analysis, the patients will be given 4 cigarettes to smoke during the next hour, and during this time the gastric analysis will be continued. At the conclusion of this hour, the patients will not smoke any more cigarettes, but the gastric analysis will be continued for an additional hour to see if there are any delayed effects. It will, of course, be important to have control studies done to be sure that merely the presence of the tube itself is not a stimulant.

We would also compare the basal gastric analysis of approximately 100 smokers with that of 100 non-smokers.

In addition, 50 ulcer patients would be evaluated clinically to determine whether their symptoms were aggravated by smoking cigarettes. A comparison in these patients would be made between filter and non-filter cigarettes.

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5. Detailed Plan of Procedure (cont'd)

Procedures

1. The exact procedure of the gastric analysis is as follows:

Patients are instructed to fast after 9 p.m. on the day preceding the test. On the morning of the test a Rehfuss tube is passed into the stomach. If there is any question as to the proper location of the tube, it is checked fluoroscopically. The residual gastric juice is aspirated and put into a specimen bottle marked "residuum." The patient is shown how to collect the gastric secretions and is instructed to expectorate his saliva so that it will not contaminate the gastric juice. He is then assisted in continually aspirating his stomach contents over the next hour. The basal-hour collection consists of four specimens taken at 15-minute intervals.

The gastric juice from each 15-minute period is measured for volume and titrated for free acid to the salmon pink end-point of Topfer's reagent, using 0.1 normal sodium hydroxide. The results are expressed in clinical units -- clinical units being the milliliters of 0.1 normal sodium hydroxide required to neutralize 100 milliliters of gastric juice. Milligrams of HCl are calculated as follows: clinical units x volume in ml. x 0.365. Mg. $HCl/hr.$ = sum of mg. HCl of the four 15-minute specimens.

2. The technique of gastric pepsin is as follows:

Determinations are performed on aliquots of 1-hour collections of gastric juice by the method of West, Ellis and Scott, with certain modifications. The exact procedure is as follows:

A 2.0 aliquot of diluted gastric juice (from 1:10 to 1:100 as necessary) is placed in a test tube with 0.05 ml. of 0.2% aqueous methyl orange and 0.1 ml. of 2N hydrochloric acid. Additional hydrochloric acid may be required to bring the solution to a pH of 3 or less. (If this is done, a correction is made in the subsequent calculation for the change in volume.) The acidified gastric juice is placed in a water bath at 37° C. before use. After one hour, .05 ml. of the gastric juice is transferred to a second tube, the volume is brought to 1.0 ml. with distilled water, and 1.0 ml. of acetate buffer is added. The contents of the tube are mixed thoroughly; 0.5 ml. of milk-buffer solution is added and quickly mixed; the tube is then returned to the water bath.

Timing: The test is timed from the moment the milk-buffer mixture is added. After one minute the tube is removed from the water bath, tilted and shaken slightly; the thin film remaining on the walls of the tube is then examined for casein particles. The tube is examined in this manner approximately every 10 seconds. The end point is reached when a fine precipitate begins to form, and the time is recorded. If the end point is reached in less than 80 seconds or more than 240 seconds, the test is repeated using smaller or larger amounts of gastric juice and corresponding amounts of water to bring the sample to 1.0 ml. Aliquots of 0.01 to 1.0 ml. of gastric juice may be used. In the case of 1.0 ml. samples, the test is timed for 10 minutes before a negative report is given.

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5. Detailed Plan of Procedure (cont'd)

Calculation: Results are expressed in units of gastric pepsin secreted per hour, one unit being equivalent to 0.26 ug. of crystallized pepsin (Armour). Results are calculated as follows:

$$0.1 \times \frac{V}{v24} \qquad \frac{(100)^{1.32}}{(t)} \qquad = \text{Units per hour}$$

where

V = total volume in milliliters of 24-hour
v = amount of gastric juice used in test in milliliters
t = time in seconds to the end point

3. Uropepsin: With the exception of the dilution factor, the same technic is used for determinations of 4-hour and 24-hour uropepsin excretions.

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6. Budget Plan:

Salaries		$ 10,000.
Expendable Supplies		1,000.
Permanent Equipment		
Overhead	15%	1.950
Other	Consulting Fee*	2,000.
Total		$ 14,950

*for evaluation of results and preparation of manuscript.

7. Anticipated Duration of Work:

One year.

8. Facilities and Staff Available:

Facilities: Beckman pH Meter, Model G
2 water baths
refrigerator
Gastric Secretory Laboratory, U.C. Medical Center
Collection Room, Gastrointestinal Clinic
Gastrointestinal Clinic Patients
Office space, office furniture, calculator, typewriter, telephone and index file.

9. Additional Requirements:

Budget breakdown:

Salaries	
Research Fellow (M.D.)	$4,000.00
Technician	4,000.00
Half-time secretary	2,000.00

10. Additional Information (Including relation of work to other projects and other sources of supply):

None.

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Signature /s./ J. Alfred Rider, M.D.
Director of Project

J. Alfred Rider, M.D., Ph.D.

Stanley C. Bateman
Business Officer of the Institution

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